REMARKS

Claim 9 is pending in the instant application. Claim 9 has been rejected. No new matter has been added by this amendment. Reconsideration is respectfully requested in light of the following remarks.

I. Rejection of Claims Under 35 U.S.C. §112

Claim 9 stands rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Specifically, the Examiner suggests that the term "ΔF508 mutant" is indefinite because there is no structure associated with this term. Applicants respectfully traverse this rejection.

The term ΔF508 mutant is neither unclear nor indefinite. As outlined in MPEP 2173.02, the essential inquiry pertaining to this requirement is whether the claims set out and circumscribe a particular subject matter with a reasonable degree of clarity and particularity. Definiteness of claim language must be analyzed, not in a vacuum, but in light of:

(A) The content of the particular application disclosure;

(B) The teachings of the prior art; and

(C) The claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made.

The specification at page 3, lines 15-18, teaches that a single mutation resulting in a deletion of the phenylalanine at position 508 of the CFTR protein, known as ΔF508, accounts for

approximately 67% of mutation in all CF patients. Indeed, this mutation is generally well-known in the art. For example, Wikipedia indicates that "[t]he most common mutation, called ΔF508, is a deletion (Δ) of one amino acid at position 508 in the CFTR protein." See attached definition of CFTR. In fact, the ΔF508 mutation has its own entry in Wikipedia, defining it as:

> "a specific mutation within the human genome. The mutation--a deletion of three base pairs (A, T, T) which form the codon for phenylalanine (F) at the 508 position--prevents a protein called the cystic fibrosis transmembrane conductance regulator (CFTR) from obtaining its normal position. Having two copies of this mutation, inherited from both parents, is the leading cause of cystic fibrosis (CF)." See attached definition of ΔF508.

In addition to this general reference to ΔF508 CFTR, pages 88-89 of A Dictionary of Genetics (enclosed herewith) indicates that the ΔF508 mutation is present in 60-70% of the CF chromosomes from North American Caucasians and results in a temperature sensitive defect in protein processing.

As currently presented, claim 9 reads on a cDNA encoding a mutant human CFTR protein having a deletion of the phenylalanine at amino acid position 508 (ΔF508). In a search of the ENTREZ GENE database at NCBI (www.ncbi.nlm.nih.gov), only one mRNA is listed as encoding human CFTR (*i.e.*, NM_000492.3). Likewise, only one accession number is listed for the human CFTR protein (*i.e.*, NP_000483.3). See ENTREZ GENE record for CFTR cystic fibrosis transmembrane conductance regulator (ATP-binding cassette sub-family C, member 7) [*Homo sapiens*], enclosed herewith. In both cases, *i.e.*, the deduced protein sequence of the mRNA of Accession

No. NM_000492.3 and the protein of Accession No. NP_000483.3, a phenylalanine is found at position 508. See attached GENBANK entries. As such, it would be readily clear which phenylalanine of human CFTR is being referred to in the present claim.

Applicants further note that numerous scientific references and patents discuss human ΔF508 CFTR. Indeed, a search of the NCBI PUBMED database for the keywords "human", "deltaF508", and "CFTR" identifies 420 hits. Moreover, Applicants direct the Examiner's attention to U.S. Patent No. 6,902,907, filed June 2, 1994, claims 1 and 4, which read on a F508 mutation which comprises a three base pair deletion of a DNA sequence encoding a phenylalanine corresponding to amino acid position 508 of a normal CFTR protein. In this regard, the PTO and skilled artisan have known and accepted that a ΔF508 mutant of human CFTR is a deletion of the phenylalanine at position 508 of the well-known CFTR protein.

Therefore, based upon the disclosure in the instant specification, the teachings of the prior art, and the claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made, Applicants submit that the skilled artisan would find the phrase "ΔF508 mutant" to be clear and definite as used in the presently pending claim. It is therefore respectfully requested that this rejection be reconsidered and withdrawn.

II. Rejection of Claims Under 35 U.S.C. §103

Claim 9 has been rejected under 35 U.S.C. §103(a) as being unpatentable over Moyer et al. ((Aug. 1999) *Am. J. Physiol.* 277(2 Pt 2):F271-6) in view of Cormack et al. ((1996) *Gene* 173:33-38) further in view of Chou et al. (1991) *J. Biol. Chem.* 266:24471-24476) for the reasons of record. The basis for the Examiner's rejection is that because the metes and bound of "ΔF508 mutant human CFTR cDNA coding region" is not clear, the CFTR-GFP nucleic acid of Moyer et al. meets the limitation of the claim. Applicants respectfully traverse this rejection.

For the reasons explained in the discussion of the rejection under 112, second paragraph, it is clear that a mutant human CFTR protein having a deletion of the phenylalanine at amino acid position 508 (ΔF508) was well-known in the art at the time the present invention was made such that one of skill in the art would clearly understand the metes and bounds of the present claim. As such, the CFTR of Moyer et al. is not the human ΔF508 CFTR-GFP of the present invention. Likewise, none of the secondary references teach or suggest this ΔF508 CFTR-GFP protein.

Under 35 U.S.C. §103, the factual inquiry into obviousness requires a determination of: (1) the scope and content of the prior art; (2) the differences between the claimed subject matter and the prior art; (3) the level of ordinary skill in the art; and (4) secondary considerations. *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1, 17-18, 148 USPQ 459, 467 (1966).

Accordingly, because the combined teachings of Moyer et al., Cormack et al. and Chou et al. fail to teach or suggest the use of

a cDNA encoding a ΔF508 mutant human CFTR, these references cannot be held to make the present invention obvious. Reconsideration and withdrawal of this rejection is therefore respectfully requested.

III. Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,

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